NOTES TO FORM PCT/ISA/220

These Notes are intended to give the basic instructions concerning the filing of amendments under Article 19. The Notes are based on the requirements of the Patent Cooperation Treaty, the Regulations and the Administrative Instructions under that Treaty. In case of discrepancy between these Notes and those requirements, the latter are applicable. For more detailed information, see also the *PCT Applicant's Guide*, a publication of WIPO.

In these Notes, "Article," "Rule" and "Section" refer to the provisions of the PCT, the PCT Regulations and the PCT Administrative Instructions, respectively.

INSTRUCTIONS CONCERNING AMENDMENTS UNDER ARTICLE 19

The applicant has, after having received the international search report and the written opinion of the International Searching Authority, one opportunity to amend the claims of the international application. It should however be emphasized that, since all parts of the international application (claims, description and drawings) may be amended during the international preliminary examination procedure, there is usually no need to file amendments of the claims under Article 19 except where, e.g. the applicant wants the latter to be published for the purposes of provisional protection or has another reason for amending the claims before international publication. Furthermore, it should be emphasized that provisional protection is available in some States only (see *PCT Applicant's Guide*, Volume I/A, Annexes B1 and B2).

The attention of the applicant is drawn to the fact that amendments to the claims under Article 19 are not allowed where the International Searching Authority has declared, under Article 17(2), that no international search report would be established (see *PCT Applicant's Guide*, Volume I/A, paragraph 296).

What parts of the international application may be amended ?

Under Article 19, only the claims may be amended.

During the international phase, the claims may also be amended (or further amended) under Article 34 before the International Preliminary Examining Authority. The description and drawings may only be amended under Article 34 before the International Preliminary Examining Authority.

Upon entry into the national phase, all parts of the international application may be amended under Article 28 or, where applicable, Article 41.

When ? Within 2 months from the date of transmittal of the international search report or 16 months from the priority date, whichever time limit expires later. It should be noted, however, that the amendments will be considered as having been received on time if they are received by the International Bureau after the expiration of the applicable time limit but before the completion of the technical preparations for international publication (Rule 46.1).

Where not to file the amendments ?

The amendments may only be filed with the International Bureau and not with the receiving Office or the International Searching Authority (Rule 46.2).

Where a demand for international preliminary examination has been/is filed, see below.

How ? Either by cancelling one or more entire claims, by adding one or more new claims or by amending the text of one or more of the claims as filed.

A replacement sheet must be submitted for each sheet of the claims which, on account of an amendment or amendments, differs from the sheet originally filed.

All the claims appearing on a replacement sheet must be numbered in Arabic numerals. Where a claim is cancelled, no renumbering of the other claims is required. In all cases where claims are renumbered, they must be renumbered consecutively (Section 205(b)).

The amendments must be made in the language in which the international application is to be published.

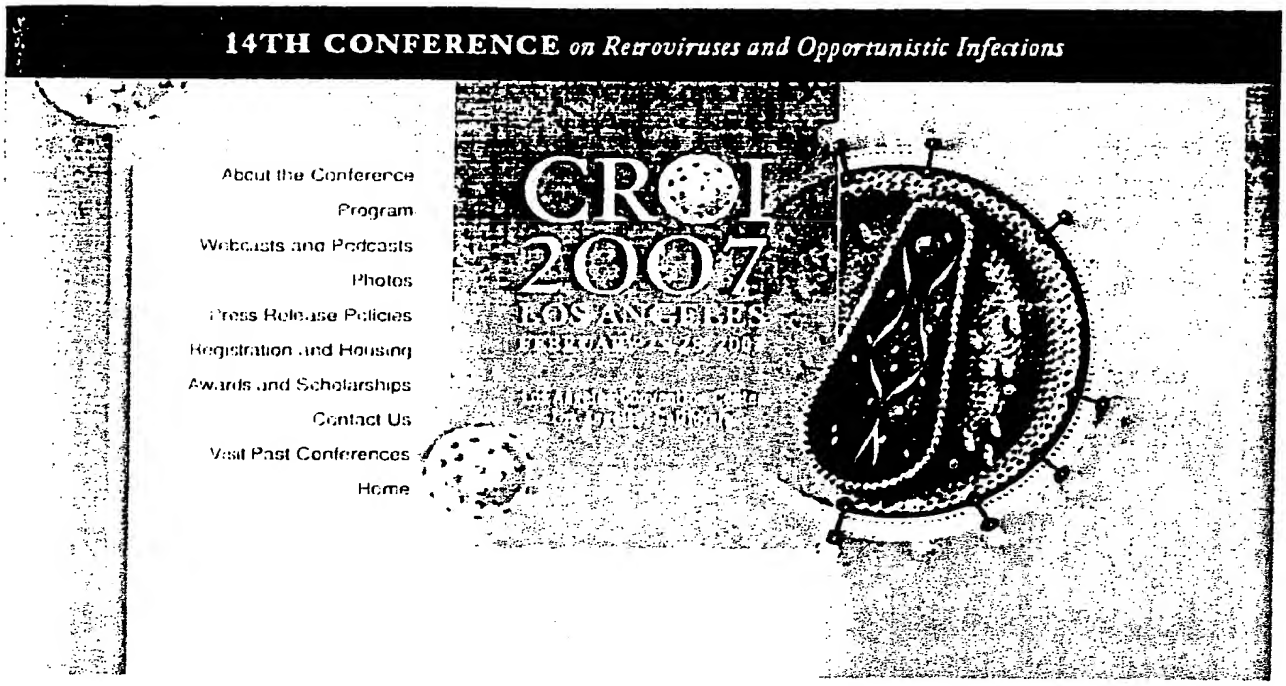
What documents must/may accompany the amendments ?

Letter (Section 205(b)):

The amendments must be submitted with a letter.

The letter will not be published with the international application and the amended claims. It should not be confused with the "Statement under Article 19(1)" (see below, under "Statement under Article 19(1)").

The letter must be in English or French, at the choice of the applicant. However, if the language of the international application is English, the letter must be in English; if the language of the international application is French, the letter must be in French.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14TH CONFERENCE *on Retroviruses and Opportunistic Infections*

Session 33 *Oral Abstracts*
Late Breaking Phase III Trials of New Antiretrovirals
Session Day and Time: Tuesday, 6:30 - 7:10 pm
Presentation Time: 6:30 pm
Room: West Hall B

104aLB
Efficacy and Safety of Maraviroc plus Optimized Background Therapy in Viremic, ART-experienced Patients Infected with CCR5-tropic HIV-1 in Europe, Australia, and North America: 24-Week Results

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[1]Chelsea and Westminster Hosp, London, UK; [2]Universitaetsklinik Köln, Germany; [3]Pfizer Global R&D, Sandwich, UK; [4]Hosp San Raffaele, Milan, Italy; [5]Ctr Hosp Univ St Pierre, Brussels, Belgium; [6]Szpital Zakazny Centrum Diagnostyki i Terapii AIDS, Warsaw, Poland; and [7]Pfizer Global R&D, New London, CT, US

Background: MOTIVATE 2 is 1 of 2 ongoing, double-blind, placebo-controlled, phase 2b/3 studies assessing the safety and efficacy of the novel CCR5 antagonist maraviroc (MVC), in treatment-experienced HIV-infected patients. These are the results of a planned interim analysis at week 24.

Methods: Triple-class-experienced patients (±triple-class resistance) with HIV-1 RNA ≥5000 copies/mL and only R5 virus (Trofile assay) were randomized 1 : 2 : 2 to receive placebo or MVC (300-mg dose equivalent) once or twice daily plus optimized background therapy (OBT) (3 to 6 ART drugs ± low-dose ritonavir). When OBT contained a protease inhibitor (PI) (other than tipranavir) and/or delavirdine, MVC 150 mg once or twice daily was administered; otherwise 300 mg once or twice daily was used. The primary endpoint was the mean change in HIV-1 RNA from baseline to week 24.

Results: Of 475 patients randomized, 464 received ≥1 dose of study drug. Baseline[†] characteristics were similar across treatment arms. Baseline median CD4 count (174, 174, and 182 cells/mm^3) and mean HIV-1 RNA (4.89, 4.87, and 4.84 $\log_{10}$ copies/mL) were also similar in the placebo, MVC once daily, and MVC twice daily arms, respectively. OBT contained ≤2 active drugs in 66.0, 62.6, and 62.3% of patients in the placebo, MVC once daily and MVC twice daily arms, respectively. Adverse events, severe adverse events, AIDS-defining events, and laboratory abnormalities (including liver enzyme abnormalities) occurred with similar frequency in the 3 treatment groups. The following analyses are based on all randomized patients who received ≥1 dose of study drug:

	Placebo+OBT (*n* = 91)	MVC Once Daily + OBT (*n* = 182)	MVC Twice Daily + OBT (*n* = 191)
Mean change in viral load from baseline* ($\log_{10}$ copies/mL)	−0.93	−1.95	−1.97
Treatment difference −placebo (97.5% CI)	N/A	−1.02 (−1.43, −0.62)	−1.04 (−1.44, −0.64)
% <400 copies/mL	23.1%	55.5%	61.3%
p value vs placebo	N/A	<0.0001	<0.0001
% <50 copies/mL	20.9%	45.6%	40.8%
p value vs placebo	N/A	<0.0001	0.0005

Mean change in CD4 from baseline[2] (cells/mm^3) p value vs placebo (95%CI)	+64 (n = 90) N/A	+112 (n = 180) <0.001 (+22, +74)	+102 (n = 185) <0.001 (+12, +64)
Category C AIDS-defining events, n	11	17	11
Discontinuations due to adverse events, n (%)	2 (2.2)	9 (4.9)	7 (3.7)
Deaths*, n (%)	0	4 (2.2)	4 (2.1)

[1]Mean of all pre-dose assessments
[2]Last Observation Carried Forward
[3]Discontinuations=no change from BL
*No deaths were related to study drug according to investigators

Conclusions: In this treatment-experienced population, MVC (twice or once daily) + OBT provided significantly superior virologic control and increases in CD4 cell count compared with placebo + OBT. There were no clinically relevant differences in the safety profile between the MVC (twice or once daily) + OBT and placebo + OBT treatment groups.

PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY

To:
JOHN P. WHITE
COOPER & DUNHAM LLP
1185 AVENUE OF THE AMERICAS
NEW YORK, NY 10036

PCT

NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL SEARCH REPORT AND THE WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY, OR THE DECLARATION

(PCT Rule 44.1)

Applicant's or agent's file reference 77840-A-PCT/JPW/BB	Date of mailing *(day month year)* 15 AUG 2008 **FOR FURTHER ACTION** See paragraphs 1 and 4 below
International application No. PCT/US 08/05564	International filing date *(day/month/year)* 30 April 2008 (30.04.2008)
Applicant PROGENICS PHARMACEUTICALS, INC.	

1 ☒ The applicant is hereby notified that the international search report and the written opinion of the International Searching Authority have been established and are transmitted herewith.

Filing of amendments and statement under Article 19:
The applicant is entitled, if he so wishes, to amend the claims of the international application (see Rule 46):

When? The time limit for filing such amendments is normally two months from the date of transmittal of the international search report.

Where? Directly to the International Bureau of WIPO, 34 chemin des Colombettes 1211 Geneva 20, Switzerland, Facsimile No.: +41 22 740 14 35

For more detailed instructions, see the notes on the accompanying sheet.

2. ☐ The applicant is hereby notified that no international search report will be established and that the declaration under Article 17(2)(a) to that effect and the written opinion of the International Searching Authority are transmitted herewith.

3. ☐ **With regard to the protest** against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:

☐ the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.

☐ no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

4. **Reminders**

Shortly after the expiration of **18 months** from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in Rules 90*bis*.1 and 90*bis*.3, respectively, before the completion of the technical preparations for international publication.

The applicant may submit comments on an informal basis on the written opinion of the International Searching Authority to the International Bureau. The International Bureau will send a copy of such comments to all designated Offices unless an international preliminary examination report has been or is to be established. These comments would also be made available to the public but not before the expiration of 30 months from the priority date.

Within **19 months** from the priority date, but only in respect of some designated Offices, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase **until 30 months** from the priority date (in some Offices even later); otherwise, the applicant must, **within 20 months** from the priority date, perform the prescribed acts for entry into the national phase before those designated Offices.

In respect of other designated Offices, the time limit of **30 months** (or later) will apply even if no demand is filed within 19 months.

See the Annex to Form PCT/IB/301 and, for details about the applicable time limits, Office by Office, see the *PCT Applicant's Guide*, Volume II, National Chapters and the WIPO Internet site.

Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-3201	Authorized officer: Lee W. Young PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774

Form PCT/ISA/220 (January 2004)

(See notes on accompanying sheet)